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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/783,786

02/20/2004

David M. Kranz

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23713 7590 03/26/2007
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EXAMINER

GUZO, DAVID

ART UNIT

PAPER NUMBER

1636

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

03/26/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/783,786

Applicant(s)

KRANZ ET AL.

Examiner

David Guzo

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 January 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-83 is/are pending in the application.
- 4a) Of the above claim(s) 11-24, 38-49 and 56-81 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10, 25-37, 50-55, 82-83 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 February 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 6/16/06; 2/23/06; 7/20/04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

Detailed Action

Applicant's election with traverse of Group I, Claims 1-10, 25-37, 50-55, 82 and 83 in the reply filed on 1/10/07 is acknowledged. The traversal is on the ground(s) that all claims in Groups I-IX relate to high affinity T cell receptors (TCRs) and as a search for this concept is required for all groups, a burdensome search is not an issue. This is not found persuasive because each of the different Groups is drawn to a patentably distinct method of using TCRs (i.e. methods of identifying ligands for TCRs, methods of killing pathogen infected cells with TCRs coupled to toxins) or methods of cloning high affinity TCRs or compositions such as soluble TCRs or DNAs encoding TCRs, etc. Each Group would require a separate search of the art which would not be co-extensive with a search of the other groups. For example, a search of methods of cloning TCRs would not be co-extensive with a search of methods of treating diseases using TCRs.

The requirement is still deemed proper and is therefore made FINAL.

Claims 11-24, 38-49, 56-81 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/10/07.

Priority for the claimed invention is granted back to the filing date of the 60/169,179 provisional application (12/06/1999).

The Continuing Data for this application is confusing. The Continuing Data indicates that the 09/009,388 application (filed 1/20/1998) claims the benefit of the provisional application 60/169,179 (filed 12/06/1999). It is unclear how an earlier filed application (the '388 application) can claim priority to a later filed application (the '179 provisional application)? Perhaps applicants mean to recite:

This application is a divisional of United States application Serial No. 09/731,242, filed December 6, 2000, which is a continuation-in-part of United States Application No. 09/009,388, filed January 20, 1998, **and wherein this application** also claims the benefit of U.S. Provisional Application No. 60/169,179, filed December 6, 1999.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-32 and 50-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim methods for using high affinity TCRs (defined by applicants as reading on engineered TCRs with stronger binding to a target ligand than the wild-type TCR) to detect ligands wherein said method comprises the steps of: labeling high affinity TCRs; contacting said labeled high affinity TCRs with ligands; detecting the

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presence of the label thereby detecting the ligand to which the labeled high affinity TCR is bound wherein the high affinity TCR exhibits a dissociation constant for the ligand greater than about 10^7 or about 10^7 to about 10^{10} . Applicants also claim a method of binding a high affinity TCR to a cell carrying a selected peptide/MHC ligand on the cell surface which comprising the steps of: providing a mutant TCR exhibiting a dissociation constant of greater than about 10^7 (or about 10^7 to 10^{10}) for the selected peptide/MHC ligand; labeling the high affinity TCR; contacting the labeled high affinity TCRs with a sample containing cells carrying one or more peptide/MHC ligands on the cell surface to bind the high affinity TCRs to selected peptide/MHC ligands present in the sample. The claims read on methods comprising generation and use of a genus of high affinity TCRs exhibiting a dissociation constant of greater than about 10^7 (or about 10^7 to 10^{10}) for the selected ligand.

Applicants do not disclose in the instant application, as can best be determined, the claimed methods wherein the high affinity TCR exhibits a dissociation constant for the ligand greater than about 10^7 or about 10^7 to about 10^{10} .

The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed invention.

In the instant case, applicants do not apparently recite any engineered high affinity TCRs with the recited dissociation constants. It would appear that each of the TCRs would have to be engineered (i.e. mutated) and the dissociation constants for any given ligand determined empirically. The instant application and the prior art do not provide any guidance as to how the protein structure of TCRs can be manipulated so as to generate TCRs with the recited dissociation constants for any given ligand. While applicants can assay the dissociation constants for high affinity TCRs – ligand combinations, such assays do not satisfy the written description requirement of 35 USC 112, 1st paragraph because applicants have not provided a disclosure sufficient for the skilled artisan to envision a representative number of species sufficient to describe the claimed genus. Applicants do not provide a structure-function relationship between the structures of the high affinity TCRs and their function of having dissociation constants in the recited ranges for any given ligand. The skilled artisan would therefore conclude that applicants were not in possession of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 25-32, 50-55 and 82-83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 25 and 33 (and dependent claims) are vague in that it is unclear what ligands applicants are attempting to identify. Applicants claim use of high affinity TCRs

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to "identify ligands". The high affinity TCRs are defined by applicants as being TCRs which have been engineered (i.e. mutated) to have higher affinity for their cognate ligand than the wild-type TCR. Since the high affinity TCRs are designed to bind to their cognate ligand at higher affinities than the wild-type TCR, it is unclear if the high affinity TCRs are used here to identify their cognate ligand or any (undefined) ligand.

Claims 4 and 6 (and dependent claims) are vague in that applicants recite "[l]abeling said high affinity TCRs with **a label that binds to the selected peptide/MHC ligand** (emphasis added)". It is unclear whether applicants mean to recite labeling a TCR which binds to the selected peptide/MHC ligand or **a label** which binds to the selected peptide/MHC ligand?

Claim 7 (and dependent claims) are vague in the recitation of the phrase "[c]ontacting said high affinity TCR with cells". Two different high affinity TCRs are recited in the claim, a high affinity TCR and a labeled high affinity TCR. It is assumed that applicants mean to recite contacting the labeled high affinity TCR with the cells.

Claim 10 is vague in that applicants recite a label that binds to specific peptide/MHC ligands, it is assumed that applicants mean to refer to a labeled high affinity TCR which binds to the ligand.

Claims 25-26 and 50-55 (and dependent claims) are vague because applicants recite dissociation constants of 10^7 or 10^7 to 10^{10} but do not recite any units of measurement with these numbers.

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The closest prior art is exemplified by Shusta et al. (JMB, 1999, Vol. 292, pp. 949-956) and Kieke et al. (PNAS, 1999, Vol. 96(10), pp. 5651-5656), both cited by applicants. Both references teach mutation of TCRs and yeast expression of said TCRs but neither teaches generation of high affinity TCRs, labeling said TCRs and using said TCRs to identify ligands.


No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Guzo
March 17, 2007


DAVID GUZO
PRIMARY EXAMINER